Journal of Student Nursing Research

Volume 1 *2007-8*
Issue 2

Article 2

9-9-2008

Long Term Quality-of-Life Outcomes in Pediatric Bone Cancer: A Systematic Review

Susan J. Paul
University of Pennsylvania

Long Term Quality-of-Life Outcomes in Pediatric Bone Cancer: A Systematic Review

Abstract

Purpose: To evaluate the current evidence on quality-of-life (QOL) outcomes for survivors of pediatric bone cancer in the lower extremities and to ascertain whether limb-sparing surgery does indeed bestow an advantage to these survivors.

Methods: A thorough search of the literature was conducted. Inclusion criteria were as follows: (a) published in the last 10 years in English, (b) focused upon patients diagnosed when they were < 25 years of age, and (c) focused on QOL and functional outcomes in pediatric bone cancer patients who underwent either limb-sparing surgery or amputation in their course of treatment.

Results: Sixteen articles were found that fulfilled all inclusion criteria. No significant differences in QOL outcomes were found. However some differences were found in functional outcomes when pediatric bone cancer survivors were compared by tumor site. Survivors with more proximal tumors had better functional outcomes with limb-sparing sparing surgery than their counterparts with amputation.

Conclusions: Future nursing research should focus on interventions to improve short and long term QOL in these patients, as no studies were found that addressed potential interventions.

Long Term Quality-of-Life Outcomes in Pediatric Bone Cancer: A Systematic Review

Susan J. Paul

Abstract

Purpose: To evaluate the current evidence on quality-of-life (QOL) outcomes for survivors of pediatric bone cancer in the lower extremities and to ascertain whether limb-sparing surgery does indeed bestow an advantage to these survivors.

Methods: A thorough search of the literature was conducted. Inclusion criteria were as follows: (a) published in the last 10 years in English, (b) focused upon patients diagnosed when they were ≤ 25 years of age, and (c) focused on QOL and functional outcomes in pediatric bone cancer patients who underwent either limb-sparing surgery or amputation in their course of treatment.

Results: Sixteen articles were found that fulfilled all inclusion criteria. No significant differences in QOL outcomes were found. However some differences were found in functional outcomes when pediatric bone cancer survivors were compared by tumor site. Survivors with more proximal tumors had better functional outcomes with limb-sparing sparing surgery than their counterparts with amputation.

Conclusions: Future nursing research should focus on interventions to improve short and long term QOL in these patients, as no studies were found that addressed potential interventions.

Every year in the United States, approximately 650-700 children and adolescents under 20 years of age will be diagnosed with bone cancer (Gurney, Swensen & Bulterys, 1999). This number accounts for 6% of all pediatric cancers diagnosed annually (Gurney et al.). Congruent with many pediatric cancers, recent advances in treatment methods have resulted in increased five-year survival rates for bone cancers. The 1975-84 survival rate of 49% increased to 63% during the years 1985-94 (Gurney et al.). While improved treatment means more survivors, it also indicates that practitioners must now give more consideration to potential long term sequale for these survivors than ever before.

For the majority of the 20th Century amputation was the treatment for bone cancer (Enneking, 2000). However, in the late 1980s and early 1990s, limb-sparing surgery gained wide recognition in the pediatric bone cancer community as being the best possible guarantor of positive long term QOL outcomes (Nagarajan, Neglia, Clohisy & Robison, 2002). There is agreement that limb-sparing surgery bestows an advantage when the tumor location is in an upper extremity. However this clarity is lost when the tumor location is in a lower extremity (Nagarajan et al.). Practitioners are just beginning to study this QOL assertion and evaluate if limb-sparing surgery provides better QOL outcomes over amputation. This review seeks to evaluate the current evidence on QOL outcomes for survivors of pediatric bone cancer in the lower extremities and to ascertain whether limb-sparing surgery affords an advantage to these survivors, as has been postulated in the past.

The two most common types of malignant bone tumors are osteosarcoma and Ewing's sarcoma, accounting for 56% and 34% of bone tumors in children, respectively (Gurney et al., 1999). Of these, 57% of tumors are found in the long bones of the lower extremities. There is a significant difference in location incidence between osteosarcoma and Ewing's sarcoma. Ewing's sarcoma is more prevalent in the central body axis (45%), while only affecting the lower extremities 29% of the time. However, 78% of osteosarcomas are found in the lower extremities (Gurney et al.).

The current model of care for children with bone cancer combines (a) chemotherapy with surgery (Nagarajan et al., 2002), with the chemotherapeutic agents and surgical interventions depending on tumor type, location and aggressiveness; (b) the child's age at diagnosis; and (c) their skeletal maturity (National Comprehensive Cancer Network, 2007). Some children with bone cancer still undergo amputation and most occur in those patients with a tumor in the

distal femur (Nagarajan et al.). Depending upon the tumor site, however, transtibial (below-the-knee), knee disarticulation, and hip disarticulation amputations can be performed in addition to transfemoral amputations (Nagarajan et al.).

Rotationplasty, a procedure that is considered half-amputation and half-limb-sparing surgery (Grimer, 2005), is another option for patients with tumors below, directly above, or around the knee (Grimer; Nagarajan et al., 2002). It is particularly useful for young patients with immature skeletons, since the reconstructed limb will continue to grow (Grimer). In this procedure, the diseased portion of the leg is removed while all of the muscular, nervous and vascular components of the lower leg, ankle and foot are retained. This structure is then rotated 180° and reattached to the remaining femur, placing the ankle joint at the level of the contralateral knee, thus giving the patient a functional "knee" joint (Grimer; Nagarajan et al.).

The overarching theme of limb-sparing surgery is to replace the portion of the resected limb with either a graft or an implant, thus retaining the form and function of the limb as much as possible. Allografts are used almost exclusively in surgery for lower extremity tumors due to the need for weight bearing. Nevertheless, some researchers are currently looking into the possibility of using autografts (Grimer, 2005). Allografts are normally implanted in the middle of the tibia or femur, when there is no joint involvement (Nagarajan et al., 2002).

The two major types of implants are endoprosthetic implants and expanding endoprosthetic implants (Nagarajan et al., 2002). Endoprosthetic implants are normally used when a patient's joint has to be removed, to replace both bone and joint. Expanding implants are essentially the same as endoprosthetic implants, except they have the ability to lengthen over time (Nagarajan et al.). Patients with immature skeletons often use expanding implants so that the affected limb has the potential to grow in proportion to the patients' other limb. However, such growth requires surgical intervention (Nagarajan et al.).

Methods

Journals indexed in the Cumulative Index to Nursing and Allied Health Literature (CINAHL), MEDLINE and PubMed Plus were reviewed. The search terms included "bone neoplasm," "pediatrics" and "quality of life". The inclusion criteria were that articles: (a) be published in the last 10 years in English, (b) reported on patients ≤ 25 years of age, or, in cases of long term QOL assessments, populations that were diagnosed during their childhood and (c) they focused on QOL outcomes for pediatric bone cancer patients who had undergone either limb-sparing surgery or amputation in the course of their treatment.

International studies were included since these countries have similar rates of pediatric bone cancer to the United States, according to Parkin, Whelan, Ferlay and Strom (2005); it appears that treatment standards are similar internationally to the standards used in the United States (Kumta, et al., 2002; Saeter, 2007 "Ewing's sarcoma"; Saeter, 2007 "Osteosarcoma"; Varan, et al., 2007). In fact, some countries utilize the treatment standards published by National Cancer Institute as their own (National Cancer Institute, 2007). This similarity allows comparison of the results of long term QOL outcomes research based both internationally and in the United States.

Results

Of 144 articles returned via the search terms listed previously, 16 articles fulfilled all inclusion criteria (see Table 1). Of these, four assessed QOL through a self-administered survey, eight were case-control, three included a physical exam with the survey and one was the proceedings of a conference. No randomized-controlled trials were found, since randomizing limb-sparing surgery and amputation in this patient population would be far from ethical.

Although a majority of the studies were based in the United States (n = 9), the rest represent a wide selection of international scientific research. Three of the studies were conducted in Germany. The rest hailed from: Sweden, Italy, Austria, England and the Netherlands. Due to the nature of treatment for pediatric bone cancers, the current QOL research focuses on two major variables: function and QOL. To maintain clarity, these two outcome measures will be discussed separately.

Functional Outcomes

Overall, limb-sparing surgery has been shown to

have better functional outcomes versus amputation with proximal tumors (Pardasaney, Sullivan, Portney & Manking, 2006; Frances, Morris, Arkader, Nickolic & Healey, 2007). This difference in long term function is not seen, however in tumors of the distal leg, especially when the knee joint is retained or when a rotationplatsy is performed (Hillmann, Hoffmann, Gosheger, Krakal & Winkelmann, 1999; Nargarajan et al., 2002; Pardasaney et al., 2006). The study conducted by Pardasaney et al. looked at differences in functional outcome for patients by comparing cases by surgical site (e.g., above or below the knee). This study of 408 patients found no difference in functional outcome for patients with below the knee surgery. However, there was a functional advantage in patients with limb-sparing procedures when the surgical site was more proximal. Pardasaney et al. found that the risk of walking with a limp was significantly greater in patients with above the knee amputations ($p = 0.005$).

A study by Hillmann et al. (1999), which compared 33 patients with rotationplasty and 34 patients with endoprosthetic replacement, found that overall, patients with rotationplasty had higher functional scores ($p = 0.47$). There did not appear to be any psychosocial disadvantage to receiving a rotationplasty. They also found that both groups of patients were satisfied with their procedure and had equally good gait and maximum walking distance. However, patients with endoprosthetic replacement needed more assistive walking devices ($p < 0.001$) than the patients with rotationplasty (Hillmann et al). Similar studies conducted in Münster, Germany and the Netherlands concluded that the functional benefits of rotationplasty were supported by the lack of negative psychosocial sequale (Rödl, Pohlmann, Gosheger, Lindner & Winkelmann, 2002; Veenstra, Sprangers, Van Der Eyken & Taminiau, 2000).

Veenstra et al. (2000) recruited 33 patients over 16 years of age who were at least one year post-surgery. These patients had high functional outcomes, wore their prosthesis for the entire day, and were satisfied with the fit of their device. Unlike the Veenstra et al. and Hillmann et al. (1999) studies, Rödl et al. (2002) assessed long term outcomes in patients with rotationplasty. They administered a weighted scale of contentment to 22 patients at least 10 years post-treatment completion and found no differences between the contentment of the studied patients and their West German contemporaries ($n = 1,688$).

In one study of 528 former participants in the Childhood Cancer Survivor Study (Nagarajan et al., 2004), no significant differences were found between 192 survivors who had undergone limb-sparing surgery and the 336 who had received amputations. In fact, the authors felt there was clear evidence that amputees do well in the long run, contrary to some earlier hypotheses. Another study used the Musculoskeletal Tumor Society (MSTS) score to rate functional outcomes of 124 patients. Although the limb-sparing group of 102 patients had improved function, when MSTS scores were compared, this elevation was not perceived by the patients (Zahlten-Hinguranage, Bernd, Ewerbeck & Sabo, 2004).

In case-control studies, survivors of pediatric bone cancer are generally found to have decreased levels of function when compared with healthy counterparts (Novakovic, Fears, Horowitz, Tucker & Wexler, 1997; Hoffman, Saltzman, & Buckwalter, 2002; Gerber, et al., 2006). Gerber, et al. tested 32 survivors' functional status, using a variety of laboratory measurements as well as self-administered surveys of functional perception and compared the participants' results with the normed values for the tools used. They found that survivors had significantly increased weakness (19 subjects with grip strength > 1 SD below normal), which positively correlates with longevity. Motor and process scores – the subjects were asked to perform basic tasks and were scored based upon their performance of those tasks – were also significantly below normal for survivors ($p < 0.001$) (Gerber, et al.). Another study reported that, in 35 survivors with transfemoral amputation, decreases in functional outcome (when compared to 35 healthy controls) was exacerbated for older survivors ($p = 0.075$) and for survivors who were older at the time at amputation ($p = 0.029$) (Hoffman, et al.). Interestingly, in a study comparing 144 osteosarcoma survivors with 61 giant cell tumor survivors, osteosarcoma survivors were significantly more likely to classify themselves as disabled and felt more limited in their functioning ($p < 0.02$) (Mankin, Gunnoe, Farid, Hornicek & Gebhardt,

2004).

Quality-of-Life Outcomes

No differences were found in QOL outcomes for the patients participating in studies that specifically compared limb-sparing surgery and amputation (Frances, et al., 2007; Nagarajan, et al., 2004; Nagarajan, et al., 2003; Zahlten-Hinguranage, et al., 2004). One study of 124 bone cancer survivors utilized the Life Satisfaction Questionnaire, which is a QOL tool that assigns higher weight to survey topics that participants rate as being more important to them (Zahlten-Hinguranage, et al.), and found that survivors were satisfied with their lives and had high QOL scores.

Another study, conducted by Frances, et al. (2007), recruited 44 patients recently diagnosed with bone cancer and administered the Pediatric Outcomes Data Collection Instrument at the time of the index procedure and annually thereafter for at least one year (average = 3 years; range = 1 to 7 years). The study found that most of the improvement in QOL was seen in the two years immediately following the index procedure. They also found that patients reported a wide range of QOL scores, highlighting the individuality of patients and perhaps that some patients still struggled with adjusting to their post-procedural functional level (Frances, et al.).

Veenstra, et al. (2000) chose to focus their article on 33 patients who had received a Van Ness-Borggreve rotationplasty. The authors found that the participants, who were over 16 years of age and at least one year post-surgery, had high psychosocial QOL outcomes (Veenstra et al.). Both men and women had QOL scores that were comparable when analyzed with healthy population norm values (95% Confidence Interval [CI] 64.8 92.9 for women and 95% CI 66.1 85.8 for men) (Veenstra et al.).

Another study looked at outcomes for 144 osteosarcoma patients when compared with 61 patients with Giant cell tumor (Mankin et al., 2004). This investigation found that the marriage rate for patients with osteosarcoma was lower than their counterparts ($p < 0.02$) (Mankin et al.). In fact, two studies reviewed found a relationship between marriage rate and overall QOL in bone cancer survivors (Mankin, et al.; Felder-Puig, et al., 1998).

Intriguingly, when Felder-Puig, et al. (1998) studied 60 bone cancer survivors they found this marriage association only seemed to correlate to QOL in survivors who had been diagnosed during adolescence. A study conducted by Elkin, Phipps, Mulhern and Fairclough (1997) highlights this peculiarity. They administered the Symptom Checklist-90-Revised to a group of 161 survivors of numerous pediatric cancers (including leukemias, Hogdkin disease, non-Hogdkin lymphoma, sarcomas and other solid tumors) who were disease-free, at least five years from diagnosis and two years from therapy completion. The authors found a significantly low level of psychological distress ($p < 0.001$) and an absence of psychopathology in a group primarily composed of adolescents.

Case-control studies were also found with a focus on QOL outcomes. The largest of these included 694 previous participants of the Childhood Cancer Survivor Study, and a random sampling of 2,667 full biologic siblings of participating survivors, found that higher education was a significant predictor for all outcome measures ($p < 0.001$) (Nagarajan et al., 2003). They found that male gender was predictive of employment ($p = 0.029$), while female gender was predictive of insurance coverage ($p = 0.003$) and being married at least once ($p = 0.004$). Novakovic, et al. (1997) also performed a case-control study comparing survivors with siblings. They found that in 89 Ewing's sarcoma survivors participants rates of employment, marital status ($p < 0.01$) and fertility ($p < 0.01$) were all significantly lower when compared with 97 siblings (Novakovic et al.). Despite this, survivors did not have ongoing health problems and generally self-identified as being in good health.

Boman & Bodegård (2004) found, in their case-control study, that among the 30 participants, those with more education had significantly better psychological coping skills ($p = 0.004$). They also discovered that a decreased ability to cope with their illness significantly related to survivors continuing to live with their parents ($p = 0.03$). Hoffman, et al., 2002 focused solely on 35 patients admitted for transfemoral amputation and then compared them with a healthy group of 35 people recruited from the local drivers' license office. They found that cases were generally similar to controls for

most QOL measures. This was the only study found that addressed the financial burden of amputation – buying and maintaining a prosthetic limb. The study found that the mean cost to do so was $4,225 per year (calculated in 1998 dollars), which would certainly impact QOL (Hoffman, et al.).

One case study discussion was included – this discussion took place during a meeting of the Tumor Board of the Pediatric Oncology Unit of the Istituto Nazionale Tumori in Milano, Italy (Ferrari, et al., 2002). The board discussed the relatively new practice of including a clinical psychologist in the treatment team of patients undergoing an amputation as treatment for bone cancer. In anecdotal reports, it was found that formal psychological support, both from medical staff and the clinical psychologist, encouraged positive psychological outcomes in pediatric patients undergoing amputation or another disfiguring or disability surgery (Ferrari, et al.).

Discussion

A review of the literature was conducted to determine the long term QOL outcomes for survivors of pediatric bone cancer and whether undergoing limb-sparing surgery or amputation correlate with specific QOL outcomes. There was a clear difference in functional outcomes. Patients who underwent limb-sparing surgery have better function in the long term. This finding, however, was only seen in patients with tumors above the knee. In patients with tumors below the knee, the functional outcomes of amputees and patients with limb-sparing procedures were very similar. Clearly the pediatric bone cancer survivors' functional outcomes were related to their course of surgical treatment.

In general, there did not appear to be a large QOL benefit for the survivors who had limb-sparing surgery over amputees. Both groups of patients had negative social and psychological sequalae, although these outcomes may be related to their cancer survivor status instead of surgical treatment. Similar results were found in a study of 417 pediatric rhabdomyosarcoma survivors (Punyko, et al., 2007). This study found that survivors were significantly less likely to have ever been married than 2,865 randomly selected age-matched siblings of Childhood Cancer Survivor Study participants ($p < 0.01$), which is fairly similar to bone cancer survivors. These findings are not similar to those of the study conducted by Meeske, Patel, Palmer, Nelson and Parow (2007), which focused on survivors of pediatric cancer in general but did not include any bone cancer survivors. Diagnoses of study participants included leukemia, Wilms' tumor, lymphoma and brain tumors, among others. They found that among 86 participants between 8 and 18 years of age who had been off-treatment for a mean interval of 7.8 years, the 62 non-fatigued survivors had similar school and emotional functioning levels to healthy children, whereas fatigued survivors had lower functional levels in these two categories. When the authors compared the relative functioning of fatigued versus non-fatigued survivors, they found that the non-fatigued survivors had significantly higher school and emotional functioning ($p < 0.0001$) (Meeske et al.).

Although amputees' QOL outcomes were lower when compared to their pediatric cancer survivor counterparts, one study looking at differences in outcomes between eight traumatic amputees and 27 cancer survivor amputees found that, in general, the cancer survivors had better QOL outcomes (Boyle, Tebbi, Mindell & Mettlin, 1982). Specifically, traumatic amputees were less successful in their choice of career and educational achievement than the cancer survivors. Boyle, et al. also found that traumatic amputees wore their prostheses less often than cancer survivors.

Limitations

This review had several limitations. First, the majority of studies reported small sample size. Second, for the purpose of this study selection criteria were implemented thereby limiting the generalizability of findings to other populations. Third, many of the participants in the included studies were diagnosed from the 1970s to the 1990s; thus, the surgical techniques and chemotherapeutic agents used to combat bone cancers were different at the time of their treatment from modern modalities. Fourth, is the generally small number of pertinent studies available in the literature. Many of the studies included were internationally based, and thus the possibility is high that the restriction of included studies to those published in English may have excluded applicable studies.

Implications for Nursing

This review highlights that pediatric bone cancer survivors need continuing support from healthcare providers into their adult years. What that support should entail and when the best time for intervention are unknown factors at this time. There needs to be continuing research into the QOL outcomes for pediatric bone cancer survivors – although we now know the outcomes for children treated from the 1970s to the 1990s, we do not know the long term outcomes of modern treatment methodology. Additionally, future studies examining functional status should include clinician assessment as well as self-report. If it were found that a reproducible disparity exists between survivors' assessment of their functional status and objective measures, the reason behind this inconsistency should be investigated.

While interventions in functional outcomes are not within the scope of nursing practice (as they are mostly related to surgical and rehabilitation techniques), QOL outcomes fall squarely within nursing's purview. Some of the QOL measures mentioned previously could be utilized by nurses to assess changes in functional and psychosocial status for patients returning to clinic for follow-up visits.

Suggestions for Future Research

Nurses should convene support groups of in-patients or out-patients who have recently had either amputation or limb-sparing surgery. Nurses should assess family coping skills when faced with the decision of either limb-sparing surgery or amputation. It is also be imperative to examine the differences in financial burden of therapy between patients with limb-sparing surgeries and amputees. Other areas of inquiry could be the differences in insurance coverage for the two therapies and necessary maintenance treatments/ surgeries. To the author's knowledge, there are no studies focusing on this patient population that have been conducted by nurses. Nurses provide the majority of in-hospital care to pediatric bone cancer patients, therefore, nurses must spearhead future research into QOL interventions with this population.

In conclusion, diagnosis of pediatric bone cancer is devastating for both the patient and family members. However, with recent advances in treatment, long term survival rates are higher than ever before. QOL in these survivors, whether treated with limb-sparing surgery or amputation, is essentially equal and positive. Although more research needs to be done to fully understand the long term implications of bone cancer treatment on QOL, survivors appear to be thriving.

References

Boman, K. K., & Bodegård, G. (2004). Life after cancer in childhood: Social adjustment and educational and vocational status of young-adult survivors [Electronic Version]. *Journal of Pediatric Hematology/Oncology, 26*, 354-362.

Boyle, M., Tebbi, C.K., Mindell, E.R., & Mettlin, C.J. (1982). Adolescent adjustment to amputation. *Medical and Pediatric Oncology, 10,* 301-312.

Elkin, T. D., Phipps, S., Mulhern, R. K., & Fairclough, D. (1997). Psychological functioning of adolescent and young adult survivors of pediatric malignancy [Electronic Version]. *Medical & Pediatric Oncology, 29*, 582-588.

Enneking, W.F. (2000). An abbreviated history of orthopaedic oncology in North America [Electronic Version]. *Clinical Orthopaedics and Related Research, 374,* 115-124.

Felder-Puig, R., Formann, A. K., Mildner, A., Bretschneider, W., Bucher, B., Windhager, R., et al. (1998). Quality of life and psychosocial adjustment of young patients after treatment of bone cancer [Electronic Version]. *Cancer, 83*, 69-75.

Ferrari, A., Clerici, C.A., Spreafico, F., Casanova, M., Massimino, M., Luksch, R., et al. (2002). Psychological support in children and adolescents with cancer when amputation is required [Electronic Version]. *Medical & Pediatric Oncology, 38,* 261-265.

Frances, J. M., Morris, C. D., Arkader, A., Nikolic, Z. G., & Healey, J. H. (2007). What is quality of life in children with bone sarcoma? [Electronic Version]. *Clinical Orthopaedics & RelatedResearch, 459*, 34-39.

Gerber, L. H., Hoffman, K., Chaudhry, U., Augustine, E., Parks, R., Bernad, M., et al. (2006). Functional outcomes and life satisfaction in long-term survivors of pediatric sarcomas [Electronic Version]. *Archives of Physical Medicine & Rehabilitation, 87*, 1611-1617.

Gurney, J.G., Swensen, A.R. & Bulterys, M. (1999). Malignant bone tumors. In Ries, L.A.G., Smith, M.A., Gurney, J.G., Linet, M., Tamra, T., Young, J.L. & Bunin, G.R. (Eds.), *Cancer incidence and survival among children and adolescents: United States SEER program 1975-1995* (National Cancer Institute, NIH Publication No. 99-4649, pp. 99-110). Retrieved November 7, 2007, from http://seer.cancer.

gov/publications/childhood/bone.pdf

Grimer, R.J. (2005). Surgical options for children with osetosarcoma [Electronic Version]. *Lancet Oncology, 6,* 85-92.

Hillmann, A., Hoffmann, C., Gosheger, G., Krakal, H., & Winkelmann, W. (1999). Malignant tumor of the distal part of the femur or the proximal part of the tibia: Endoprosthetic replacement or rotationplasty [Electronic Version]. *Journal of Bone and Joint Surgery. 81-A,* 462-468.

Hoffman, R. D., Saltzman, C. L., & Buckwalter, J. A. (2002). Outcome of lower extremity malignancy survivors treated with transfemoral amputation [Electronic Version]. *Archives of Physical Medicine & Rehabilitation, 83*, 177-182.

Kumta, S.M., Cheng, J.C.Y., Li, C.K., Griffith, J.F., Chow, L.T.C., Quintos, A.D. (2002). Scope and limitations of limb-sparing surgery in childhood sarcomas [Electronic Version]. *Journal of Pediatric Orthopaedics, 22,* 244-248.

Mankin, H. J., Gunnoe, J., Farid, Y., Hornicek, F. J., & Gebhardt, M. C. (2004). Long-term effects of connective tissue cancer treatment [Electronic Version]. *Clinical Orthopaedics & Related Research,* (426), 74-86.

Meeske, K.A., Patel, S.K., Palmer, S.N., Nelson, M.B., & Parow, A.M. (2007). Factors associated with health-related quality of life in pediatric cancer survivors [Electronic Version]. *Pediatric Blood Cancer, 49,* 298-305.

Nagarajan, R., Clohisy, D. R., Neglia, J. P., Yasui, Y., Mitby, P. A., Sklar, C., et al. (2004). Function and quality-of-life of survivors of pelvic and lower extremity osteosarcoma and Ewing's sarcoma: The childhood cancer survivor study [Electronic Version]. *British Journal of Cancer, 91*, 1858-1865.

Nagarajan, R., Neglia, J. P., Clohisy, D. R., & Robison, L.L. (2002). Limb salvage and amputation in survivors of pediatric lower-extremity bone tumors: What are the long-term implications? [Electronic Version]. *Journal of Clinical Oncology, 20,* 4493-4501.

Nagarajan, R., Neglia, J. P., Clohisy, D. R., Yasui, Y., Greenberg, M., Hudson, M., et al. (2003). Education, employment, insurance, and marital status among 694 survivors of pediatric lower extremity bone tumors: A report from the childhood cancer survivor study [Electronic Version]. *Cancer, 97*, 2554-2564.

National Cancer Institute. (2007). *Osteosarcoma and malignant fibrous histiocytoma of bone.* Retrieved November 28, 2007, from http://www.meb.uni-bonn.de/Cancernet/107864.html

National Comprehensive Cancer Network. (2007). *NCCN clinical practice guidelines in oncology: Bone cancer.* Retrieved November 28, 2007, from http://www.nccn.org/professionals/physician_gls/PDF/bone.pdf

Novakovic, B., Fears, T. R., Horowitz, M. E., Tucker, M. A., & Wexler, L. H. (1997). Late effects of therapy in survivors of Ewing's sarcoma family tumors [Electronic Version]. *Journal of Pediatric Hematology/Oncology, 19*, 220-225.

Parkin, D.M., Whelan, S.L., Ferlay, J., & Storm, H. (2005). Cancer incidence in five continents, Vol. I to VIII. *International Agency for Research on Cancer CancerBase No. 7.* Retrieved November 5, 2007 from http://www-dep.iarc.fr/

Pardasaney, P. K., Sullivan, P. E., Portney, L. G., & Mankin, H. J. (2006). Advantage of limb salvage over amputation for proximal lower extremity tumors [Electronic Version]. *Clinical Orthopaedics & Related Research, 444*, 201-208.

Punyko, J.A., Gurney, J.G., Baker, K.S., Hayashi, R.J., Hudson, M.M., Liu, Y., et al. (2007). Physical impairment and social adaptation in adult survivors of childhood and adolescent rhabdomyosarcoma: A report from the childhood cancer survivors study [Electronic Version]. *Psycho-Oncology, 16,* 26-37.

Rödl, R. W., Pohlmann, U., Gosheger, G., Lindner, N. J., & Winkelmann, W. (2002). Rotationplasty--quality of life after 10 years in 22 patients [Electronic Version]. *Acta Orthopaedica Scandinavica, 73*, 85-88.

Saeter, G. (2007) Ewing's sarcoma of bone: ESMO clinical recommendations for diagnosis, treatment and follow-up [Electronic Version]. *Annals of Oncology*, *18 (2)*, ii79-ii80.

Saeter, G. (2007) Osetosarcoma: ESMO clinical recommendations for diagnosis, treatment and follow-up [Electronic Version]. *Annals of Oncology*, *18 (2),* ii77-ii78.

Varan, A., Yazici, N., Aksoy, C., Gedikoğlu, G., Yalçin, B., Akyüz, C., et al. (2007). Treatment results of pediatric osteosarcoma: Twenty-year experience. *Journal of Pediatric Orthopaedics, 27,* 241-246.

Veenstra, K. M., Sprangers, M. A., van der Eyken, J. W., & Taminiau, A. H. (2000). Quality of life in survivors with a Van Ness-Borggreve rotationplasty after bone tumour resection [Electronic Version]. *Journal of Surgical Oncology, 73*, 192-197.

Zahlten-Hinguranage, A., Bernd, L., Ewerbeck, V., & Sabo, D. (2004). Equal quality of life after limb-sparing or ablative surgery for lower extremity sarcomas[Electronic Version]. *British Journal of Cancer, 91*, 1012-1014.

***Author Highlight**

Susan Paul is a senior undergraduate nursing student at the University of Pennsylvania.